

and more or less tinnitus; (2) where the vestibule was involved simultaneously with the cochlea, producing, as a rule, occasional attacks of vertigo in addition to symptoms arising from disease of the cochlea; (3) where the vestibular nerve alone was affected and where all symptoms indicating disease of the labyrinth might be absent, except for possible occasional attacks of vertigo. The progress of the disease differed widely in different cases. There might be a gradual increasing degeneration of the parts involved; the progress of the degeneration might be accelerated by acute exacerbations; or the acute attacks might be followed by a long period of quiescence. Primary degeneration of the labyrinth was not infrequently a complication of syphilis, hereditary or acquired. It was also observed as a sequel of the infectious fevers, especially mumps, typhoid, measles and scarlet fever. In a large percentage of cases, however, the etiology was not accounted for. It was in these cases that focal infection was suggested as a possible cause. The similarity between the manner in which the labyrinth involvement took place and the involvement of other nerves in which focal infection was known to be the cause, suggested this conclusion.

Concussion Injury of the Ear.—SHUTER (*Jour. Laryngol., Rhinol. and Otol.*, London, February, 1918) states that he has seen a large number of cases on different fronts, and differentiates between machine gunners and concussion deafness; in the former there are more frequently instances of deafness, in the latter a more general lowering of the whole tone scale, they occur more commonly in cases of preëxisting middle-ear disease, and are due not to acoustic concussion but to the pressure waves caused by a shell explosion, as by the explosion of a German mine in a confined space, in trench cases and after proximate bomb explosions, rendering the patient temporarily unconscious and inappreciative of sound for forty-eight hours. These causes are presented for secondary examination, sometimes months after the injury, with the following combination of symptoms, marked decrease in hearing, by bone conduction, tinnitus, paraësis, better aërial hearing in a quiet room and hearing tones of low pitch aërially better in proportion than tones of high pitch.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Histopathology of Muscle in Gas Gangrene: Contusion, Ischemia and Infection.—RENE SAND (*Ambulance de l'Océan*) discusses the various pathological changes in the structure of muscles in gas gangrene under the three following heads: (1) lesions due to mechanical cause; (2) lesions due to circulatory disturbances; (3) lesions caused by toxic

infection. In his studies he has endeavored to avoid three very common errors, *i. e.*, he did not restrict himself to cases of gas gangrene but made comparative studies, noting the alterations due to direct compression of muscle as well as those due to gas gangrene. In the matter of technic he advises the use of frozen sections rather than those embedded in paraffin, for he believes that in the latter process the muscle suffers a distortion of its fibers, an effacing of transverse striations with a dissociation of myofibrils. His third care was in the matter of cutting out the blocks for study to avoid disfiguring the form and structure of the muscle elements. Of the 50 cases studied the author never found fatty degeneration or infiltration, amyloid or calcareous deposits in the tissues. Of the lesions produced by shock at a distance, contusion, compression or incision, he found the following changes occurred: (1) interstitial hemorrhages, interstitial ecema and edema of the muscle fibers; (2) loss of transverse striations with greater clearness of longitudinal markings; (3) hyperplasia of the nuclei of the sarcolemma; (4) necrosis of muscle fiber. The majority of these alterations are temporary, not found after fourteen days. In the lesions due to circulatory disturbances, total ischemia, ischemia and lymphatic stasis by compression for several hours and prolonged total ischemia with severing of nerve (Volkman's disease), he observed characteristic changes. At the beginning there was edema of the muscle fibers, with slight interstitial edema, then total necrosis of the muscle and connective tissue and finally the muscle fiber lost all semblance of structure and became a flaky mass. In the third group we find a study of cases of toxic infection in which the characteristic changes are a hyaline degeneration of the connective tissue and muscle fibers and necrosis and fragmentation of the latter. The typical lesions of gas gangrene are hemolysis, hyaline degeneration and necrosis of connective tissue and muscle fibers. It may be that a preliminary contusion is essential for the development of gas gangrene, but the extension of the lesion is the function of the bacillus; where there is no *Bacillus perfringens* there is no gangrene. The microorganism becomes embedded in the interstitial tissue; it fastens itself on the muscle fiber and by its toxins produces degeneration and necrosis of the fiber and penetrates farther only when this fiber is in a state of entire disintegration and death. The action of the toxins of *Bacillus perfringens*, he claims, is incontestable. The reabsorption of the toxic products engendered by the disintegration of muscle brings about certain visceral disturbances, notably nephritis.

Experimental Acute Nephritis.—GOTO (*Jour. Exper. Med.*, 1918, xxvii, 413) supplemented an earlier work on experimental uranium nephritis, with further investigations, using cantharidin, arsenic, diphtheria toxin and potassium chromate subcutaneously in the dog. All animals were carefully controlled for at least two days before the poisons were administered. Albumin and casts appeared promptly in the urine of those dogs receiving cantharidin, arsenic and potassium chromate, whereas their appearance in the urine was delayed for two days when diphtheria toxin was used. Histologically, sections of the kidneys of the different dogs showed varying degrees of congestion of the blood-vessels and convoluted tubules, with granular degeneration of the

epithelium of the convoluted tubules as well as granular plugs in the lumina. In addition, the diphtheria toxin produced shrunken glomeruli and a finely granular material in the capsular spaces. Biochemical determinations were carried out on the blood. The results showed a retention of non-protein and urea nitrogen and chlorides, along with a moderate acidosis. These findings were more marked in the cases of diphtheria and chromate nephritis. The author noted from his experiments, however, that the degree of retention of non-protein and urea nitrogen in the blood varied considerably in different dogs receiving the same dose per kilo of a given poison. A second series of investigations was undertaken to ascertain the effect of sodium bicarbonate upon the course of a milder nephritis produced by the same substances. The sodium bicarbonate was given by stomach tube, for several days, at a constant hour each day. The milder degree of nephritis was gained by giving a smaller dose than was employed in the first series, where almost all the dogs died. It was found that sodium bicarbonate, given in this way, diminishes the acidosis, but that, histologically, the grade of nephritis was apparently unchanged. Little or no effect was noted upon the degree of retention of nitrogen and of chloride in the blood.

The Action of Antiseptics on the Toxin of *Bacillus Welchii*. In the recent studies on the use of antiseptics it has been shown that they are valuable not only in removing bacteria from contaminated wounds, but also in destroying the toxins of the microorganisms. TAYLOR and AUSTIN (*Jour. Exper. Med.*, 1918, xxvii, 375) carried out a series of experiments upon the toxins of the *Bacillus Welchii*, using pigeons as the indicator for the potency of the toxin-antiseptic mixtures. The toxin was gained by anaerobically growing the microorganisms on special media. The toxin was standardized and then treated with certain antiseptic solutions. The mixture after remaining in contact for five minutes was injected into the pigeon. In this manner it was found that Dakin's solution and chloramine-T will destroy the toxin of *Bacillus Welchii*. The authors believe that similar destruction of the toxin will occur *in vivo*, as was demonstrated by them *in vitro*. Phenol solutions did not exhibit this effect. Pigeons could be protected against multiple lethal doses of the toxin by the addition of the antiseptic solution.

Cultivation Experiments on the Globoid Bodies of Poliomyelitis.—Owing to the technical difficulties offered in the identification of the globoid bodies isolated from cases of poliomyelitis by Flexner and Noguchi, many investigators have been unable to confirm their results. SMILLIE (*Jour. Exper. Med.*, 1918, xxvii, 319), fully cognizant of the problems involved, has undertaken a simpler and more successful method. Poliomyelitis was produced in rhesus or cynomolgus monkeys by virus inoculated intracranially, intranasally or hematogenously. After the disease had reached its height the animals were etherized and small sterile pieces of cerebrum, cord, liver, spleen, kidney or thymus were put into sterile test-tubes into which a sterile piece of rabbit kidney had been placed. About 15 c.c. of sterile, clear, bile-free, relatively fresh, warm, ascitic fluid of no less than 1015 specific gravity were then added. Complete anaerobiosis was obtained by the hydrogen-

nitrogen jar. As many as twenty-five tubes were placed in each jar and incubated for eleven or twelve days. The second generation was made by taking 0.2 c.c. of fluid from the first and subculturing it in other ascitic-kidney media. In addition 0.1 c.c. was planted in tubes containing a semisolid medium. At least five subsequent generations were made. The same criteria as used by Flexner and Noguchi were employed for the determination of the globoid bodies. In all eighteen monkeys were used. In the first 4 vacuum jars were used and the results were unsatisfactory. The material from 3 other monkeys showed streptococci, which the author regarded as agonal invaders. Of the remaining 11, typical globoid bodies were obtained from 7, with a total of twenty-two strains. The largest number of strains per monkey was six; 2 gave only one strain. Nineteen of the completely isolated strains were obtained from the brain, one from the cervical cord and two from the spleen. Eleven completely isolated cultures were encountered. No positive diagnosis was made unless the globoid bodies were found under at least five different fields. Twenty-eight days was the shortest period of time, after the primary inoculation of the media, which was required for a positive diagnosis, while the longest time was fifty-four days. No definitely positive culture was ever found in the first generation. It was found in another series of experiments that the globoid bodies were unable to attack even the simple sugars. Eight different strains which had been isolated by the author were inoculated into healthy monkeys. Three of the animals exhibited some degree of paralysis after intracranial and intraspinal injection. None of the cultivated strains produced typical poliomyelitis. The author concluded from this that very few cultures retain sufficient pathogenicity to cause poliomyelitic infection in monkeys.

Extracts of Antibodies Obtained from Specific Precipitates of Typhoid-antityphoid Serum Complex.—Recently, evidence has been produced to show that large doses of a bactericidal serum administered for therapeutic effect can and often does give rise to "serum sickness." In order to obtain antibodies in a solution as free from foreign protein as possible, WEINSTEIN (*Jour. Immunology*, 1918, iii, 17) precipitated the antibodies from antityphoid serum by a specific antigen, later dissociating the antigen-antibody complex. The agglutinin content of a highly potent antityphoid serum was used as the indicator of a specific antibody. Owing to the resistance of *Bacillus typhosus* to autolysis the method of Chickering in making pneumococcus antigen was found to be unsatisfactory. The author obtained the best results by digesting the bacteria in a 2.5 per cent. solution of antiformin, neutralizing with normal HCl, purifying with absolute alcohol and dissolving in normal saline. Equal quantities of such an antigen and antityphoid serum gave the maximum precipitate, which contained, besides precipitins, agglutinins, complement-fixing, bactericidal and protective bodies. The diluted antigens appeared to be more efficacious than the undiluted. By slightly alkalinizing the solution, 5 per cent. of the agglutinins, 50 per cent. of the bactericidal and 60 per cent. of the complement-fixing bodies could be precipitated, whereas strong alkaline solutions promptly destroyed all antibodies. The optimum temperature was 42° C., and there was apparently no advan-

tage in incubating the mixture longer than one hour. Successive washings of the precipitate reduced the agglutinin content. The author was able to confirm the work of Chantemesse and Widai by using simultaneous injections of streptococcus vaccine to increase the virulence of *Bacillus typhosus*. It was learned that 1 c.c. of the anti-typhoid extract would protect guinea-pigs against a fatal dose of typhoid bouillon culture (2 c.c.) and that 0.2 c.c. of the extract would protect mice against 0.2 c.c. of the culture, also a lethal dose.

Typhoid Bacteremia during the Course of Miliary Tuberculosis.—The accurate differential diagnosis between acute miliary tuberculosis and typhoid fever has long been the bane of the clinician. The occurrence of a typhoid bacteremia in patients dying of miliary tuberculosis is as interesting as it is unusual. BLOOMFIELD (*Am. Rev. of Tuberculosis*, 1918, ii, 28) reports 2 such cases. Both individuals were colored, their ages being eight and twenty-six years respectively. Neither gave a history of typhoid fever. The boy exhibited no clinical evidence of typhoid while the adult showed sufficient signs to be regarded and treated as such. In the youth a pure culture of *Bacillus typhosus* was obtained from the blood stream on the thirteenth and nineteenth days of his illness, whereas the man showed the same organism in his circulatory system only on the tenth day. Both had a negative Widai reaction. The younger individual developed a meningitis, dying in twelve days; the older was operated upon for a perforated duodenal ulcer twenty-four days after his admission and died ten hours subsequently. At autopsy both cases showed an acute miliary tuberculosis. There were no characteristic lesions of typhoid fever to be found in any organ. The author was inclined to regard both as cases of acute miliary tuberculosis, with an accidental bacteremia of *Bacillus typhosus*. He goes on to say that a one-time carrier state would explain the source of the organisms.

A Rapid Method for the Production of Precipitin Antigen from Bacteria: An Attempt to Apply it to the Determination of the Type of *Pneumococcus* in Sputum.—KRUMWIEDE and NOBLE (*Jour. Immunology*, 1918, iii, 1) propose a method for the rapid production of an antigen from bacteria by dissolving them in antiformin, boiling, neutralizing, extracting with alcohol, diluting with normal saline, centrifuging and decanting. Emphasis is laid on boiling the suspension in antiformin. Antigens were so prepared from broth cultures of *pneumococcus* and agar cultures of *Bacillus typhosus*, types of *Bacillus paratyphosus*, *Bacillus diphtheriae* and *Bacillus mallei*. It was found that unless appropriate dilutions of antigen and sera were employed and the time factor controlled, crossed reactions were numerous and marked, particularly with closely allied organisms. Comparable results, however, were obtained when antigen prepared by the accepted method was used. An attempt to extract a typhoid antigen from the feces was unsuccessful. Antigen was then prepared from pneumonic sputum in accordance with the method above outlined. Equal quantities (0.2 c.c.) of the sputum antigen and type sera were employed and the degree of precipitation recorded. The rapidity of reaction depends, apparently, upon the strength of the antigen. Ordinarily the entire

procedure could be conducted in from one-half to one hour. Positive results were obtained in relatively few cases, although no false reactions were encountered. The authors were impressed by the fact that bacterial antigens are much stronger than serum antigens. They hope to be able to improve the method by future investigations.

Experimental Study of the Pathogenesis of Carcinoma.—YAMAGIWA and ICHIKAWA (*Jour. Can. Res.*, 1918, iii, 1) have undertaken a series of experiments in an attempt to reproduce cancer. Their procedure was to paint a solution of coal-tar upon the surface of the ears of rabbits. By continuing this application over different periods of time, varying grades of epithelial reaction were attained. The authors do not state the exact nature of the coal-tar solution nor the manner of application. Animals were treated every 2 or 3 days for 30 to 360 days. They observed that during the early stages the coal-tar acted as an irritant, inducing a hyperkeratosis. Later, after about 50 days, the hypertrophic epithelium formed elevated and even pedunculated masses. Some of these masses continued to grow after the irritant was withdrawn. As the lesion became still more chronic the epithelial proliferation showed a tendency to downward growth, with invasive qualities. Microscopic examination showed features resembling true carcinomata. They believed that true malignant growth was developed in seven instances, in four of which metastases were found in the regional lymph nodes. The description of the metastases is not clear, and in one case the extension of the new growth is rather assumed than proved. Cancer growth was only obtained in animals which had been treated over a long period of time. In the majority of instances it occurred only after the 150th day. The tissue response to the application of coal-tar differs from the experimental hyperkeratosis induced by means of Sudan III. The coal-tar lesions are primarily pedunculated outgrowths which by the authors are at times spoken of as cutaneous horns. By the procedure of these authors the importance of an irritating agent in the development of new growth is demonstrated.

Acidosis and Acid Excretion in Pneumonia.—PALMER (*Journal of Experimental Medicine*). The study of various urines demonstrates that in the absence of β -hydroxybutyric acid the hydrogen ion concentration and titratable acidity are due largely to the ratio between acid and basic phosphates. Metabolism during the febrile stage of pneumonia results in the production of considerable amounts of acid substances, and the more severe the intoxication the greater the amounts of free organic acid at the hydrogen ion concentration of 5 which are present. There is excreted in the urine of subjects ill with acute lobar pneumonia a large amount of organic acid which is free at a hydrogen ion concentration of 5. The increased ammonia and acid excretion, low carbon dioxide in the blood, diminished affinity of the blood for oxygen and retention of large amounts of alkali indicate an excessive acid production during the febrile stage of the disease. Acidosis as determined by the combined carbon dioxide in the plasma is seldom if ever severe.